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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/818,086	Applicant(s) Baskin et al.
	Examiner Joyce Tung	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 5, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-68* is/are pending in the application.

4a) Of the above, claim(s) *51-67* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-50 and 68* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-68* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The amendment filed 12/5/2003 has been entered.

2. The rejection of claims 7, 10-12, 23, and 25-50 under 35 U.S.C. 112, second paragraph in section 4(b)-4(d) is withdrawn.

a. Claims 10 and 35 remain rejected under 35 U.S.C. §112, second paragraph in section 4(a) because it is still unclear whether or not the nucleic acid from the virus or prokaryote as listed in the claims is chemically modified. Clarification is required.

b. Claims 26-50 remain rejected under 35 U.S.C. §112, second paragraph in section 4(e) because it is still unclear how the sequence of the at least one amplification product of the first reaction composition is determined since the first reaction composition does not has a fluorescence indicator. Thus, the clarification is required.

c. Claim 49 remains rejected under 35 U.S.C. §112, second paragraph in section 4(e).

Applicants argue that the recitation of "a 5'-nuclease fluorescent indicator" is described in the specification (See pg. 9, paragraph no. 24). The specification describes the 5'-nuclease fluorescent indicator is a short oligonucleotide attached by fluorescent molecules and the fluorescent indicator is broken by the 5' nuclease activity of the DNA polymerase when it is replaced by the newly polymerized strand during PCR. However, these limitations do not explicitly ~~to~~ during the fluorescent indicator itself but rather the process by which it is degraded. Thus the rejection is maintained.

3. Claims 1-25 and 68 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Pritham et al. (J of Clinical Ligand Assay, 1998, Vol.(4), pg. 404-412) in view of Johnston-Dow et al. (6,103,465).

Pritham et al. disclose a rapid PCR method to monitor the amplification by detecting the fluorescent signal (See pg. 404, the abstract) involving using fluorescence probe (See pg. 405 column 2, second paragraph and pg 406 column 2 to pg. 409, column 1). The teachings of Pritham et al. are recited through out the limitations of claims 1-9, and 19-24, except that Pritham et al do not disclose the sequencing method used to detect a specific target nucleic acid as recited in the limitations of claim 1.

Pritham et al. also do not indicate the source of the DNA sample used as listed in claims 10, 25 and 50 in the method.

Johnston-Dow et al. disclose a method for typing HLA class I gene and the method involving DNA sequencing techniques (See the Abstract and column 9, lines 9-22). The method is to provide for the specific DNA sequencing of HLA-A, HLA-B and HLA-C (See column 3, lines 19-22). Johnston-Dow et al. also disclose that any source of human nucleic acid can be used, for example, blood and lymphoblostoid cell lines (See column 6, lines 9-14) as recited in the limitations of claims 10, 25 and 50. Johnston-Dow et al. further indicate that HLA typing is performed routinely in connection with many medical indications, the study of auto-immune disease and the determination of susceptibility to infectious disease (See column 1, lines 57-62). This teaching suggests the limitations of claims 11-18 in that the pathogen will be from a virus,

prokaryote and eukaryote, the presence of the given target polynucleotide indicates the presence of the genetic disease or a specific allele which can indicate serotype.

It would have been prima facie obvious to an ordinary skill in the art at the time of the instant invention to combine the teachings of Pritham et al. and Johnston-Dow et al. to carry out the method as claimed with a reasonable expectation of success. The motivation is that the teachings of Pritham et al. indicate that fluorescent monitoring of PCR provide qualitative and quantitative information in that the qualitative information includes purity and identity (See pg. 404, column 1, last paragraph) and rapid cycle PCR is an ideal technique for fluorescence monitoring because temperature gradients within samples are minimized (See pg. 404, column 2, second paragraph) and the method of Johnson-Dow et al. is applied to the locus-specific nucleic acid amplification followed by sequence-specific detection of the amplified product for the DNA typing of HLA class I gene via DNA sequencing in that by sequencing the exons in both directions, the effect of sequencing errors on the assignment of HLA type is minimized and the method greatly reduces the number of reagents and the complexity of the sequencing protocols required (See column 9, lines 29-37).

However, Applicants argue that there is no motivation to combine the teachings of Pritham et al. and Johnston-Dow et al. to carry out the method as claimed. As discussed above, the motivation is that the teachings of Pritham et al. indicate that fluorescent monitoring of PCR provide qualitative and quantitative information in that the qualitative information includes purity and identity (See pg. 404, column 1, last paragraph) and rapid cycle PCR is an ideal

technique for fluorescence monitoring because temperature gradients within samples are minimized (See pg. 404, column 2, second paragraph) and the method of Johnson-Dow et al. is applied to the locus-specific nucleic acid amplification followed by sequence-specific detection of the amplified product for the DNA typing of HLA class I gene via DNA sequencing in that by sequencing the exons in both directions, the effect of sequencing errors on the assignment of HLA type is minimized and the method greatly reduces the number of reagents and the complexity of the sequencing protocols required (See column 9, lines 29-37).

4. Claims 26-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Pritham et al. (J of Clinical Ligand Assay, 1998, Vol.(4), pg. 404-412) in view of Johnston-Dow et al. (6,103,465) as applied to claims 1-25 and 68 above, and further in view of Wittwer et al. (6,174,670).

The teachings of Pritham et al. and Johnston-Dow et al. are set forth in section 3 above. The teachings of Pritham et al. and Johnston-Dow et al. do not indicate that there are two reaction compositions involved in the methods.

Wittwer et al. disclose methods of monitoring hybridization during polymerase chain reaction using two pairs of oligonucleotides and a nucleic acid binding fluorescent dye to monitor amplification of a selected template (See column 13, lines 62 to column 14, lines 29).

Thus, it would have been prima facie obvious to an ordinary skill in the art at the time of the instant invention to combine the teachings of Pritham et al. , Johnston-Dow et al. and Wittwer et al. to carry out the method as claimed with a reasonable expectation of success. The

motivation of combining the teachings of Pritham et al. and Johnston-Dow et al. are discussed in section 3 above and the motivation of applying the teachings of Wittwer et al. is that the method of Wittwer et al. improves the sensitivity of PCR quantification and reduces the time of fluorescence monitoring for PCR.

Summary

5 No claims are allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

J. Tung

February 4, 2003

Jeffrey Siew

JEFFREY SIEW
PRIMARY EXAMINER
2/10/03